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fulfillment of the requirements for the
degree of Master of Science.

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A THESIS

by

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Under the supervision of Dr.R.B. Sandin

Department of Chemistry

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Submitted to the Committee on
Graduate Studies, University of
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Edmonton, Alberta .

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PART I
COLCHICINE LIKE COMPOUNDS

INTRODUCTION

Colchicine is an extremely poisonous alkaloid first isolated from the autumn crocus. Investigations on colchicine were started by an incidental observation that cancer patients, who suffered from gout and who received colchicine as an adequate remedy, seemed to benefit also in respect to their tumors (1).

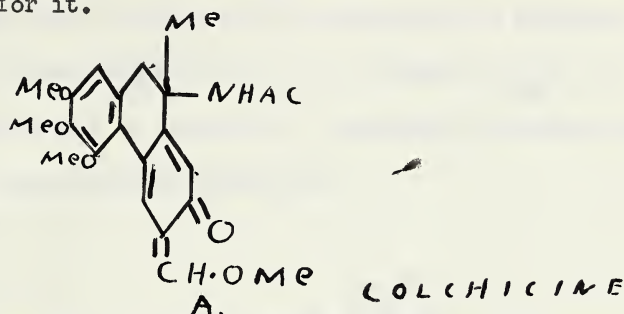
Even, in very low concentrations it arrests the process of cell divisions (mitosis) in plant or animal cells (2). Colchicine also is a growth promoter; monstrous embryos have been obtained by treating chick embryos with colchicine during the first few days of incubation.

The effect which colchicine exerts in arresting mitosis suggested that it might be useful as a chemotherapeutic agent for cancer. However, when it is administered at dose levels just sufficient to arrest mitosis, little effect upon the growth of the tumor is discerned (3). Only when the drug is administered in very large doses, just below the minimum lethal dose, is it possible to produce a partial and a temporary regression of certain kinds of tumors (3, 4). However, at such high dose levels, hemorrhage is induced in tumors and thus, regression probably occurs not directly as a result of mitotic arrest but as a result of the destruction of the newly formed capillary endothelium in the tumors.

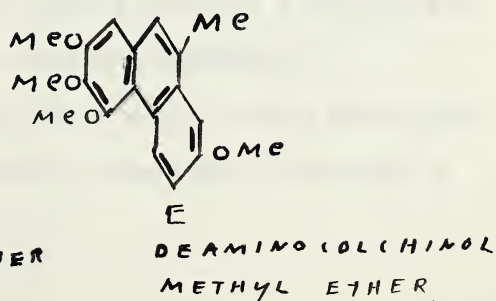
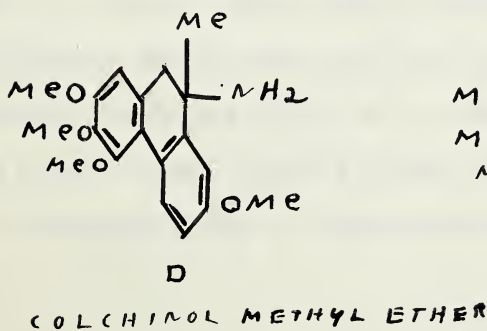
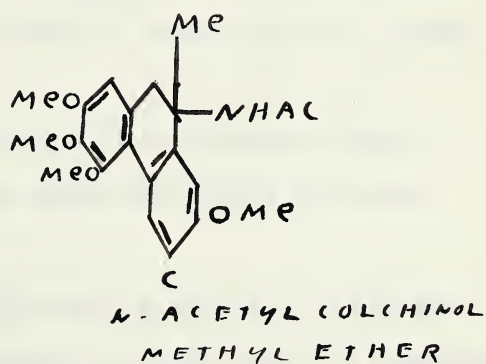
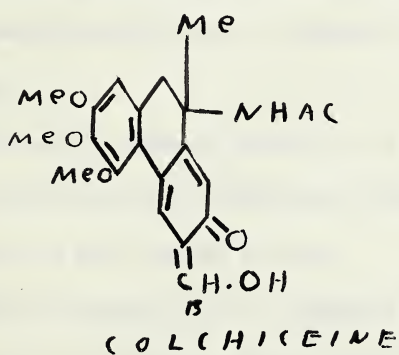
The disadvantages in the use of colchicine as a chemotherapeutic agent are due to two reasons: (1) the lack of cytological specificity in its

action, i.e., it is impossible to administer doses lethal to all the cells of a tumor without destroying essential dividing cells elsewhere in the body,
(2) the general toxicity, especially to the central nervous system.

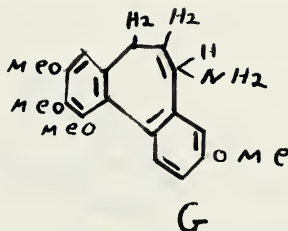
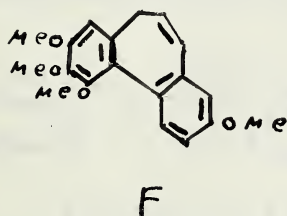
Fundamental work on the structure of colchicine was done by Windaus (5) who proposed formula A for it.



Some of the key degradation products of colchicine are illustrated by formulas B, C, D and E. Some of these compounds have been tried in the treatment of cancer but despite the fact that they are less toxic than colchicine and consequently can be used in higher doses, their effect upon the arresting of mitosis is not as great.



Recently Cohen, Cook and Roe (6) suggested that ring B in colchicine might be 7- membered rather than 6- membered. Later, evidence in favor of this idea appeared in a series of articles by Cook (7)(a, b, c, d) and also by Tarbell, Frank and Fanta (8). They showed conclusively that deaminocolchinol methyl ether could not be structure E as suggested by Windaus. It must be 9, 12, 13, 14 - tetramethoxyl- 3, 4, 5, 6 - dibenz - $\triangle^{1, 3, 5}$ cycloheptatriene as illustrated by formula F. Accordingly colchinol methyl ether probably is best represented by formula G.



Recently Lettre and co-workers (1,9) reported that 1, 2 - diphenyl-ethylamines substituted in one of the phenyl groups by at least one methoxyl group possess the ability to inhibit the mitosis of certain cells in tissue culture.

This work prompted Hartwell and Kornberg (10) to synthesize other 1, 2 - diphenyl-ethylamines containing methoxyl groups substituted in various positions in both phenyl groups.

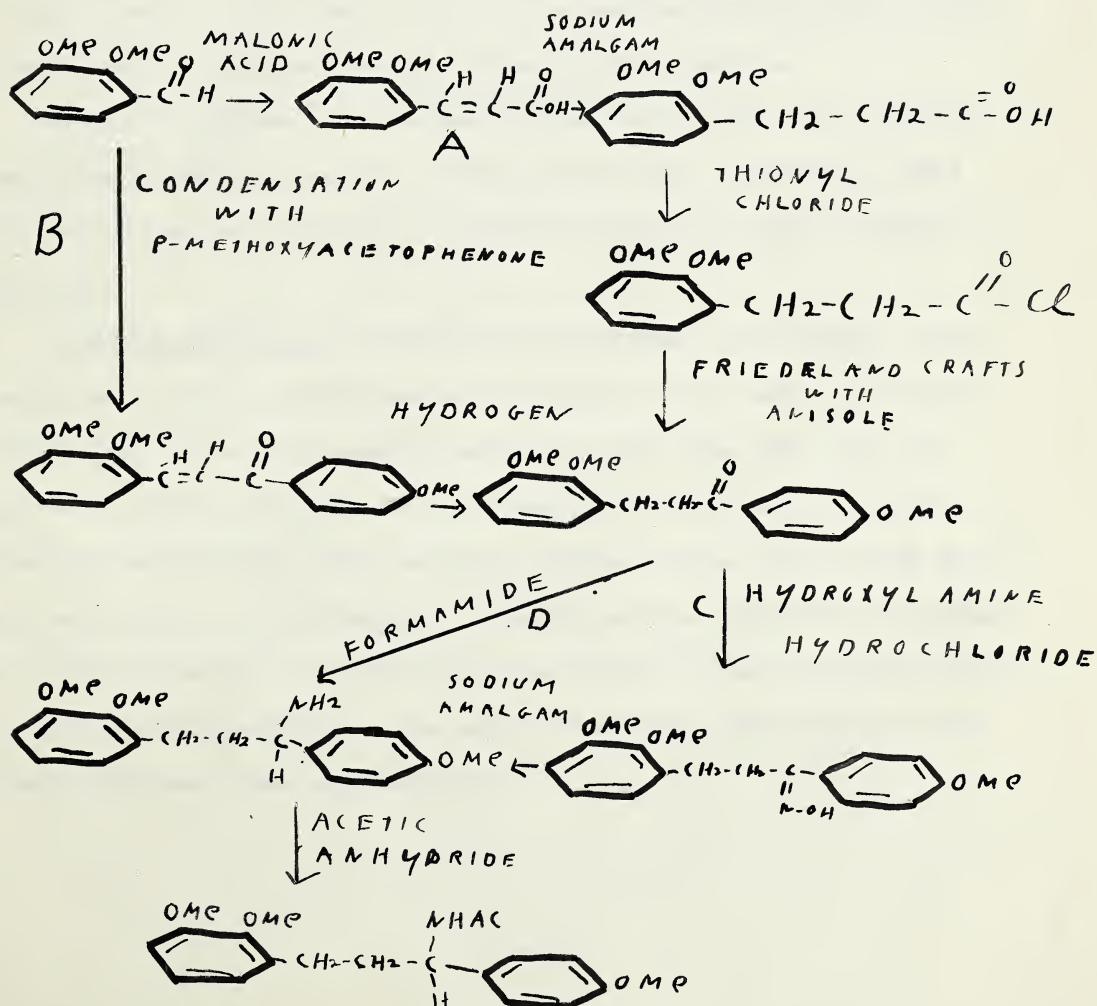
These compounds may be regarded as open-chain analogues of the Windaus structure for colchinol methyl ether. Because of the new idea of a 7-membered ring in colchinol methyl ether, the best analogue should be a derivative of 1, 3-diphenyl-propylamine and not of 1, 2-diphenyl-ethylamine.

The primary object of Part I of this thesis was to prepare derivatives of 1, 3- diphenylpropylamine in which methoxyl groups were substituted in

either or both phenyl groups. The closest structural analogue would be 1-(m-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-propylamine. It has not been synthesized as yet although an isomer of it has been isolated as the hydrochloride.

DISCUSSION

The following flow sheet illustrates the series of reactions used in the synthesis of a typical acylated-amine, N-acetyl-(p-methoxyphenyl)-3-(2,3-dimethoxyphenyl)-propylamine.



There were two possible routes available to synthesize the key "hydrochalcone" which could be changed into an amine by two methods.

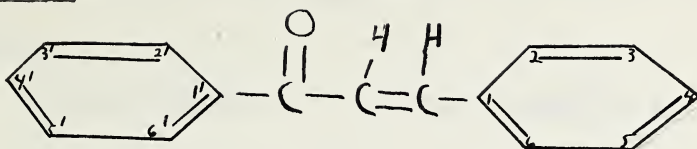
Routes A and B were both successfully employed in the synthesis of 2,3,4'-trimethoxyhydrochalcone. As route B was not as long and since yields were better, method A was not used for other compounds.

The usual procedure to go from the hydrochalcone to the corresponding amine was by route C. The oximes were readily made and could be reduced to amines by either sodium amalgam and acetic acid or by sodium and ethanol.

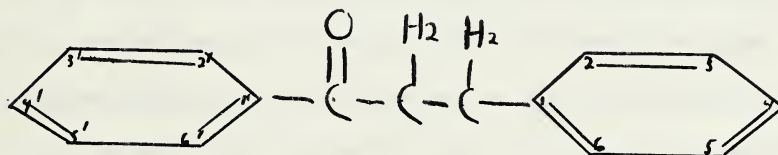
Route D utilized the Leukart reaction using formic acid and ammonia. Although this reaction gave excellent yields for unsubstituted hydrochalcone, it gave no amine in the case of 3,4,4',5-tetramethoxyhydrochalcone and only a small yield in the case of 2,3,4'-trimethoxyhydrochalcone.

None of the amines were obtained crystalline and only poor yields of the acyl-amine were obtained by refluxing with acetic anhydrides. These acyl derivatives were difficult to purify and they had a great tendency to supercool.

Aldehydes and Ketones 2,3-dimethoxybenzaldehyde, anisaldehyde, acetophenone and p-methoxyacetophenone were purchased from a commercial source. Verataldehyde was made by a method outlined in Org. Syn. Coll. Vol. II, 1943, 620. Great difficulty was encountered in the synthesis of 3,4,5-trimethoxybenzaldehyde. The Rosenmund reduction of the acid chloride gave very poor yields of the aldehyde. The method of Sonn and Muller, suggested as an alternative method by Cook (7,b) was likewise found to be unsuitable. The most successful method was the method of McFadyen and Stephans as outlined by Buchanan, Cook and Loudon (7,c).

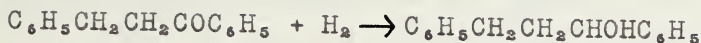
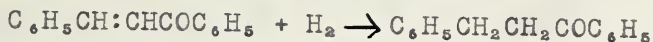
Chalcones

The parent compound chalcone is shown above, together with the system of numbering. Chalcones were produced in high yields by the condensation of equimolar amounts of aldehydes and ketones using sodium methoxide as a catalyst. This condensation took place best in the cold. If the temperature was allowed to rise, uncrystallizable oils were produced. They undoubtedly were produced by the 1,4- addition of the ketone to the chalcone. The chalcones were all beautiful yellow compounds easily purified.

Hydrochalcones

In most cases the hydrochalcones were produced by the low-pressure hydrogenation of the chalcones dissolved in acetic acid using Adam's platinum oxide as a catalyst. The color changed from the bright yellow of the chalcone to colorless for the hydrochalcone. The chalcone was shaken with hydrogen under 2-3 atmospheres until the pressure became constant. The drop in pressure was always more than the theoretical indicating that hydrogenation had gone too far and the carbonyl group had been attacked. After filtering off the catalyst and evaporating off the acetic acid, uncrystallizable oils usually were produced. They were used directly without purification to make the

oxime. The formation of oils suggested that some carbinol was produced as an impurity.



This would account for the fact that more than the theoretical amount of hydrogen was used. Later it was found that the chalcones could be reduced to hydrochalcones using ethyl acetate as the solvent. Here, only the theoretical amount of hydrogen was absorbed and the hydrochalcones could easily be purified.

One other method was used to synthesize 2,3,4'-trimethoxyhydrochalcone. 2,3-Dimethoxybenzaldehyde was converted (with high yields) into 2,3-dimethoxycinnamic by the use of malonic acid. The 2,3-dimethoxycinnamic acid was reduced to 2,3-dimethoxyhydrocinnamic acid by 4% sodium amalgam. The 2,3-dimethoxyhydrocinnamic acid was converted to the corresponding acid chloride by means of thionyl chloride and the acid chloride condensed with anisole by means of a Friedel and Crafts reaction. The 2,3,4'-trimethoxyhydrochalcone produced would not solidify but gave an oxime identical with that made from 2,3,4-trimethoxyhydrochalcone, made from the corresponding chalcone.

Oximes

The general procedure was to reflux the hydrochalcone (dissolved in pyridine and ethyl alcohol) with hydroxylamine hydrochloride for five hours. The oxime usually crystallized when the mixture was poured into ice and water. 3,4,4'-trimethoxyhydrochalcone oxime did not crystallize so the crude oxime was reduced to the amine. The fact that the oxime did not crystallize suggests that a mixture of geometrical isomers of the oxime were produced.

Hartwell and Kornberg (10) suggest that they obtained a mixture of geometrical isomers when they prepared 2,3,2',3'-tetramethoxydesoxybenzoin oxime.

Amines

The procedure generally followed for the reduction of the oxime was that of Allen and Buck (11). In all cases the free bases were not obtained crystalline. The hydrochlorides of the amines were found to be soluble in water, ethanol and even benzene. Reduction of the oxime could also be effected by sodium on a boiling solution of the oxime in absolute ethanol. It was found that a benzene extraction of an aqueous hydrochloride solution seemed to extract much of the hydrochloride which later separated from the benzene solution. 1-(p-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-propylamine could be recrystallized from benzene. The amines could not be purified by vacuum distillation, the distillate gave negligible amounts of nitrogen by micro-kjeldahl analysis and gave an odor of ammonia suggesting the amine had lost ammonia giving an unsaturated compound.

Acylated-Amines

Poor yields of acylated-amines were obtained by refluxing the amines with acetic anhydride and subsequent dilution with water. The acyl derivatives had a great tendency to supercool.

Leukart Reaction on Hydrochalcones

The general procedure as outlined by Crossley and Moore (12) was followed. The hydrochalcone was treated with a mixture of formic acid and ammonia at 160-190° for ten hours. The formyl derivative was hydrolysed by means of concentrated hydrochloric acid giving the amine hydrochloride.

This procedure gave excellent yields in the case of hydrochalcone but for derivatives of hydrochalcone the yields were very poor. Possibly the

operating conditions could be modified to give good yields of amines. The reaction has not been explored sufficiently to arrive at any definite conclusion on its applicability in synthesizing the required amines.

EXPERIMENTAL PROCEDURE

All melting ^{points} and boiling are uncorrected.

2,3,4'-Trimethoxychalcone. To a cooled solution of 16.5 g. (0.1 mole) of 2,3-dimethoxybenzaldehyde and 15.0 g. (0.1 mole) of p-methoxyacetophenone dissolved in 100 cc. of methyl alcohol was added 2.0 g. of sodium dissolved in 50 cc. of methyl alcohol. The mixture was allowed to stand at room temperature overnight and the beautiful yellow crystals were filtered and washed with ice cold methyl alcohol. The yield was 29.0g (96%). After recrystallization from ethyl alcohol the compound melted at 102-103° (reported 102-103°)(13).

2,3,4'-Trimethoxyhydrochalcone. To 48 g. of 2,3,4'-trimethoxychalcone, dissolved in 200 cc. of glacial acetic acid was added 0.1 g. of Adam's platinum oxide catalyst. The solution was shaken with hydrogen under a pressure of 2-3 atmospheres (in a low pressure catalytic hydrogenation apparatus) until the hydrogen pressure became constant. The catalyst was removed by filtration and the solvent evaporated off leaving an uncrystallizable oil. The solution which was bright yellow before the hydrogenation was colorless when the hydrogenation was over. The oil was assumed to be the required hydrochalcone and was used directly without further purification.

2,3-Dimethoxycinnamic Acid. Twenty grams of 2,3-dimethoxybenzaldehyde, 26 g. of malonic acid, 50 cc. pyridine were heated for two hours on a water bath and then boiled for fifteen minute, and poured into dilute hydrochloric acid giving 23.7 g. (92%) of crude material which melted at 178-179° (reported 180-181°)(15).

2,3-Dimethoxyhydrocinnamic Acid. Twenty-four grams of 2,3-dimethoxycinnamic acid was dissolved in 20% sodium hydroxide solution, heated to 80° and reduced with 400 g. of 4% sodium amalgam. The mixture after being filtered and acidified yielded 19.5 g. (80%) of material whose m.p. was 62-63° (reported 63°)(14).

2,3-Dimethoxyhydrocinnamoyl Chloride. Ten grams of crude 2,3-dimethoxyhydrocinnamic acid dissolved in 20 cc. of chloroform was allowed to react at room temperature for three hours with 6cc. of thionyl chloride. The solvents were removed on a water bath and the residue vacuum distilled giving 8.5 g. (75%) of 2,3-dimethoxyhydrocinnamoyl chloride, b.p. 173-174° (35 mm.) (reported 165-166°/15 mm.)(15).

2,3,4'-Trimethoxyhydrochalcone. To a well-cooled solution of 8 g. of anisole dissolved in 50 cc. of carbon disulphide was added 10 g. of anhydrous aluminum chloride. Eight and one-half grams of 2,3-dimethoxyhydrocinnamoyl chloride was added and the mixture was allowed to sit at room temperature for several hours. The mixture was then refluxed for thirty minutes and the aluminum chloride complex was hydrolysed by pouring into a mixture of ice and hydrochloric acid. The mixture was steam distilled and the residue extracted with benzene. The benzene solution was washed with dilute sodium hydroxide, then twice with water and dried over anhydrous sodium sulphate. The benzene was evaporated leaving an oil which did not solidify. It gave the same oxime as did the oil produced from the reduction of 2,3,4'-trimethoxychalcone.

2,3,4'-Trimethoxyhydrochalcone Oxime. The viscous oil produced from 48 g. of 2,3,4'-trimethoxychalcone and 12.5 g. of hydroxylamine hydrochloride, dissolved in a mixture of 100 cc. of pyridine and 100 cc. of absolute ethyl alcohol, were refluxed for five hours. The mixture was then poured into ice

and water giving an oil which solidified on standing. The yield of crude product was 27 g. After several recrystallizations from dilute ethyl alcohol the yield was 23 g. of material melting at 127-128° (reported 128°) (13).

1-(p-Methoxyphenyl)-3-(2,3-dimethoxyphenyl)-propylamine. Seventeen and one-half grams of 2,3,4'-trimethoxyhydrochalcone oxime, dissolved in 200 cc. of ethyl alcohol was treated while hot with 860 g. of 3% sodium amalgam, which was added in small portions. One hundred cubic centimetres of glacial acetic acid was added from time to time to keep the solution just acid. Sufficient water was added when needed to keep the sodium acetate formed in solution. The mixture was diluted with water and allowed to stand overnight to permit any unreduced oxime to separate out. The mercury was separated by means of a separatory funnel and the unreduced oxime was filtered off. On the addition of an excess of ammonium hydroxide an oil separated out. The solution was extracted with benzene and the benzene solution washed with water and dried over anhydrous sodium sulphate. After the benzene was removed by distillation, 12 g. of an uncrystallizable oil remained.

Some of this oil, dissolved in absolute ethanol, was treated with dry hydrogen chloride. No hydrochloride separated from the solution. Also this oil when dissolved in benzene and treated with dry hydrogen chloride gave no precipitate. This oil on being vacuum distilled came over at 260° at 6 mm. giving 8.0 g. of a viscous oil. A microkjeldahl analysis indicated no nitrogen was present and since the distillate had an ammonia odor, it was suspected that the amine broke down on being subjected to heat.

One-half a gram of the oil, dissolved in 95% ethyl alcohol, was added to 10 cc. of a saturated solution of picric acid dissolved in 95% ethyl alcohol. On heating to boiling and subsequent cooling, no picrate separated out.

N-Acetyl-1-(p-methoxyphenyl)-3-(2,3-dimethoxyphenyl)-propylamine. Twelve grams of the above oil was refluxed with an excess of acetic anhydride, diluted with water and made alkaline with sodium hydroxide. An oil separated and gradually became solid on standing. After numerous recrystallizations from dilute acetic acid there remained 2.5 g. of small glistening white crystals. This compound had a great tendency to supercool. m.p. 113.5-114.5°.

Anal. Calcd. for $C_{20}H_{25}O_4N$: C, 69.95; H, 7.34; N, 4.08. Found: C, 70.13; H, 7.29; N, 3.98.

4,4'-Dimethoxychalcone. This compound was made in a 91% yield in a similar manner to 2,3,4'-trimethoxychalcone by the condensation of anisaldehyde with p-methoxyacetophenone. m.p. 101-102°(reported 100-102°)(16).

4,4'-Dimethoxyhydrochalcone. This compound was made by the catalytic reduction of 4,4'-dimethoxychalcone analogously to the preparation of 2,3,4'-trimethoxyhydrochalcone. It could not be isolated in the crystalline form so was used directly without further purification.

4,4'-Dimethoxyhydrochalcone Oxime. This compound was prepared by the same procedure as 2,3,4'-trimethoxyhydrochalcone oxime. m.p. 117-118° (reported 119°) (17).

1,3-Di(p-methoxyphenyl)-propylamine. This amine was obtained as an oil by the reduction of the oxime by the method used for the trimethoxy compound already described.

N-Acetyl-1,3-di(p-methoxyphenyl)-propylamine. This compound was prepared by refluxing 12.0 g. of the above oil with acetic anhydride. After numerous recrystallizations from dilute acetic acid a yield of 3.0 g. of fine white crystals were obtained, melting at 114.5°.

Anal. Calcd. for $C_{19}H_{23}O_3N$: C, 72.81; H, 7.40. Found: C, 72.86; H, 7.36.

Veratraldehyde. The procedure of Silberschmidt (18) was followed. Seventy-six grams of vanillin yield 76 g. of veratraldehyde.

3,4,4'-Trimethoxychalcone. Eighty grams (86%) of this chalcone was obtained from 52 g. of veratraldehyde and 47 g. of p-methoxyacetophenone. m.p. 93-94°.

3,4,4'-Trimethoxyhydrochalcone. An uncrystallizable oil was obtained by the catalytic hydrogenation of the above chalcone. It was used directly without further purification for the preparation of the corresponding oxime.

3,4,4'-Trimethoxyhydrochalcone Oxime. This oxime could not be obtained as a solid by treating the above oil with hydroxylamine hydrochloride by the method used for 2,3,4'-trimethoxyhydrochalcone oxime. The crude oxime was reduced with sodium amalgam without further purification.

1-(p-Methoxyphenyl)-3-(3,4-dimethoxyphenyl)-propylamine. The crude amine was obtained by reducing the above oil with sodium amalgam, in a similar manner to the reduction of 2,3,4-trimethoxyhydrochalcone oxime. This amine would not crystallize on long standing.

N-Acetyl-1(p-methoxyphenyl)-3-(3,4-dimethoxyphenyl)-propylamine. The above oil on refluxing with acetic anhydride and subsequent dilution with water gave a very crude product. After numerous recrystallizations from dilute acetic acid, one-half gram of small white crystals were obtained melting at 110.5°.

Anal. Calcd. for $C_{20}H_{28}O_4N$: C, 69.95; H, 7.34. Found: C, 70.37; H, 7.39.

3,4,5-Trimethoxybenzaldehyde. This aldehyde was best obtained by the method of McFadyen and Stevens. The directions followed were those of Buchanan, Cook and Loudon (7,c).

3,4,4',5-Tetramethoxychalcone. Seventy-five grams (73%) of this beautiful yellow chalcone were obtained from 61 g. of 3,4,5-trimethoxy-benzaldehyde and 46.6 g. of p-methoxyacetophenone. After several recrystallizations from ethyl alcohol the melting point was 134-135°.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.52; H, 5.85.

3,4,4',5-Tetramethoxyhydrochalcone. Eighteen and one-half grams of the above chalcone dissolved in 150 cc. of ethyl acetate was shaken with hydrogen under 2-3 atmospheres, using 0.1 g. of Adam's platinum oxide as a catalyst. After the pressure had become constant, the platinum black was filtered off and the solutions from four such hydrogenations were combined. The material left after the ethyl acetate had been evaporated was crystallized from dilute ethyl alcohol giving 58 g. (77%) of fine white crystals which melted at 94-95°.

Anal. Calcd. for $C_{19}H_{22}O_5$: C, 69.06; H, 6.72. Found: C, 68.92; H, 6.61.

3,4,4',5-Tetramethoxyhydrochalcone Oxime. Twenty-seven grams (81%) of this oxime was produced from 32 g. of 3,4,4',5'-tetramethoxyhydrochalcone oxime by the same method used in the preparation of 2,3,4'-trimethoxyhydrochalcone oxime. After several recrystallizations from dilute ethyl alcohol the oxime was obtained as fine white needles melting at 101.5-102.5°.

Anal. Calcd. for $C_{19}H_{23}O_5N$: C, 66.07; H, 6.71. Found: C, 66.21; H, 6.77

1-(p-Methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-propylamine Hydrochloride.

Fifty grams of sodium was added in small pieces to a refluxing solution of 20 g. of 3,4,4',5-tetramethoxyhydrochalcone oxime dissolved in 500 cc. of anhydrous ethyl alcohol. The cooled solution was acidified with hydrochloric acid and extracted with 500 cc. of benzene. From this benzene solution a white compound gradually separated. After two recrystallizations from benzene the melting point was constant at 185-186°. The aqueous layer from the

benzene extraction was made alkaline with sodium hydroxide and extracted with benzene. No compound could be isolated from this benzene solution.

Anal. Calcd. for $C_{19}H_{26}O_4NCl$: Cl, 9.64. Found: Cl, 10.04.

Leukart Reaction on Hydrochalcone. The method outlined by Crossley and Moore (12) was followed.

To a three-necked flask equipped with a dropping funnel, a down directed condenser was added 83 cc. (1.25 moles) of concentrated ammonium hydroxide and 64 g. of 90% formic acid. The temperature was raised to 160° by distilling out water and 52.5 g. (0.25 moles) of hydrochalcone was added. The temperature was kept between $170-190^\circ$ for fifteen hours, after which the formyl derivative was hydrolysed by boiling with 100 cc. of concentrated hydrochloric acid. After standing overnight, the mixture was diluted with water and extracted with benzene. Forty-six grams of 1,3-diphenylpropylamine hydrochloride gradually settled from the benzene solution. The melting point of the hydrochloride after being recrystallized from dilute hydrochloric acid was 195° (reported 195°) (19).

SUMMARY

Four compounds which are derivatives of 1,3-diphenylpropylamine have been synthesized. These compounds may be regarded as open chain analogues of colchicol methyl ether. These compounds are 1-(p-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-propylamine hydrochloride, *N*-acetyl-1-(p-methoxyphenyl)-3-(3,4-dimethoxyphenyl)-propylamine, *N*-acetyl-1-(p-methoxyphenyl)-3-(2,3-dimethoxyphenyl)-propylamine and *N*-acetyl-1,3-di(p-methoxyphenyl)-propylamine.

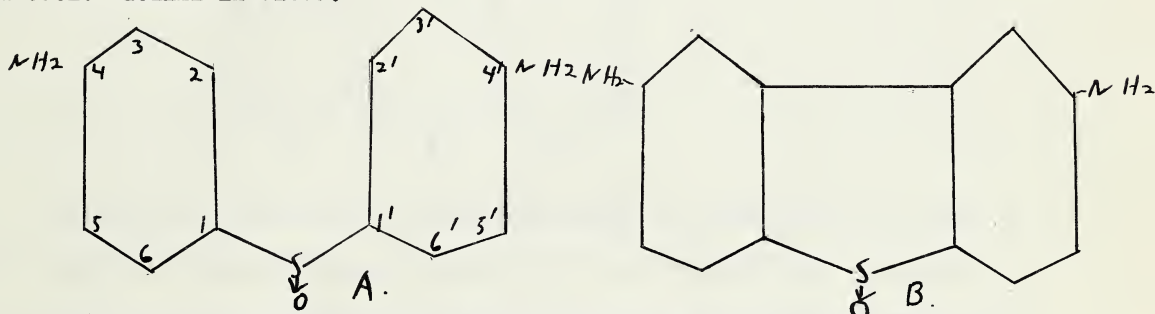
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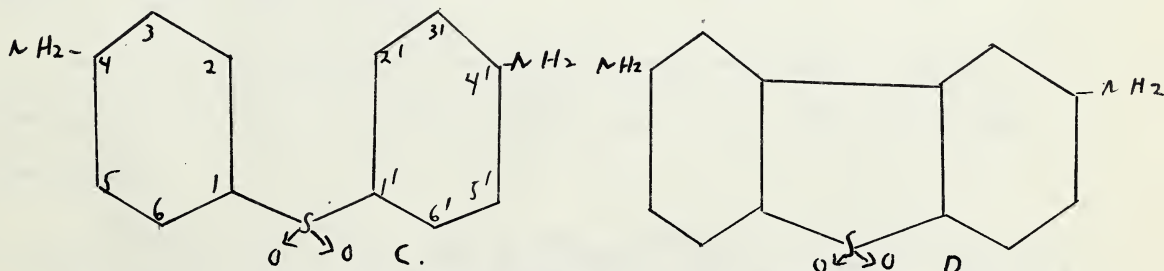
PART IIDerivatives of DibenzothiopheneIntroduction

Recently Boyland (1) found that some aromatic sulphur compounds retarded the growth of spontaneous mammary cancers in mice. This retardation ceased after the cessation of the administration of the drug being tested.

The 4,4'-diaminodiphenyl--and the 4,4'-dinitrodiphenyl--sulphides,--sulfoxides and--sulphones all showed some action, but the most effective compounds were the sulfoxides, particularly 4,4'-diaminodiphenyl-sulfoxide. 4,4'-Diaminodiphenyl-sulphone was later shown to inhibit the growth of the tubercle bacilli in vitro.



2,8-Diaminodibenzothiophene-5-oxide represented above by structure B may be considered to be derived from 4,4'-diaminodiphenylsulfoxide (represented by structure A), by direct union of the 2,2'- positions.

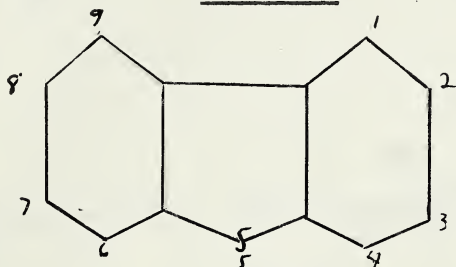


Similarly 2,8-diaminodibenzothiophene-5-dioxide, represented by structure D, may be considered to be derived from 4,4'-diaminodiphenylsulphone by a direct union of the 2,2' position.

It was thought that this modification of the open-chain compounds A and C in structures B and D might modify the properties sufficiently so that they might be useful in the chemotherapy of cancer and tuberculosis. Accordingly the object of part II of this thesis was to synthesize 2,8-diaminodibenzothiophene-5-oxide, and 2,8-diaminodibenzothiophene-5-dioxide.

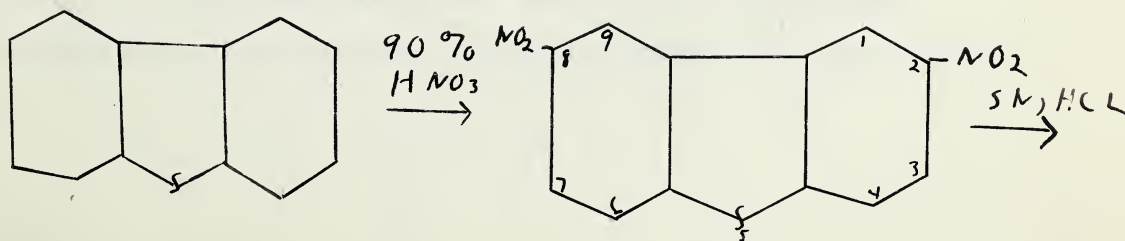
Recently 2,8-diaminodibenzothiophene-5-dioxide was synthesized by Neumoyer and Amstutz (2), so efforts along that line were abandoned. All attempts to synthesize the corresponding sulphoxide have so far failed.

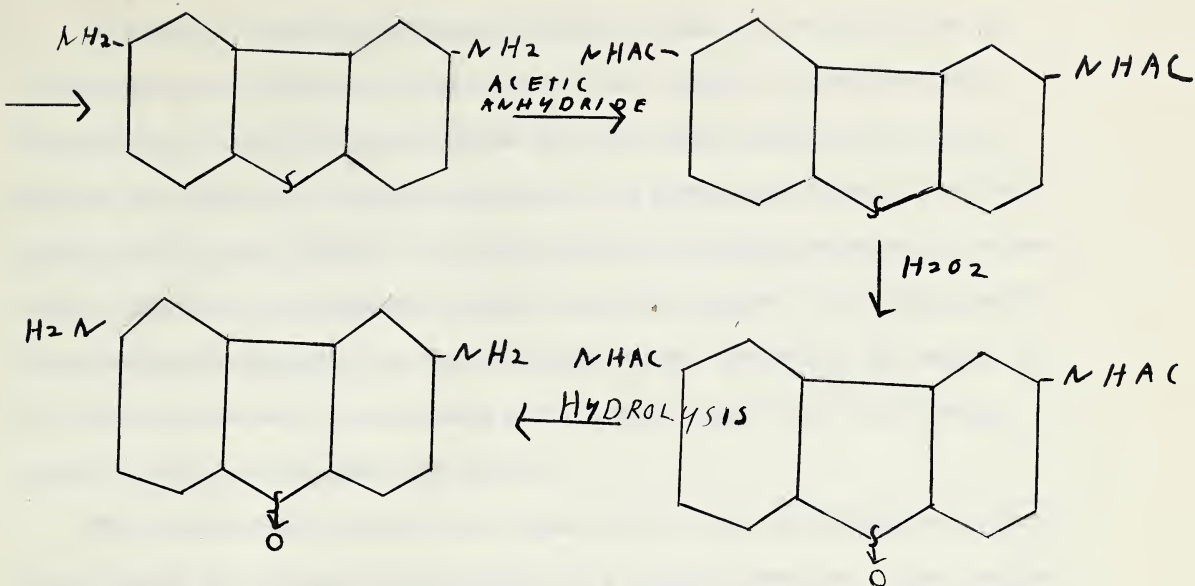
Discussion



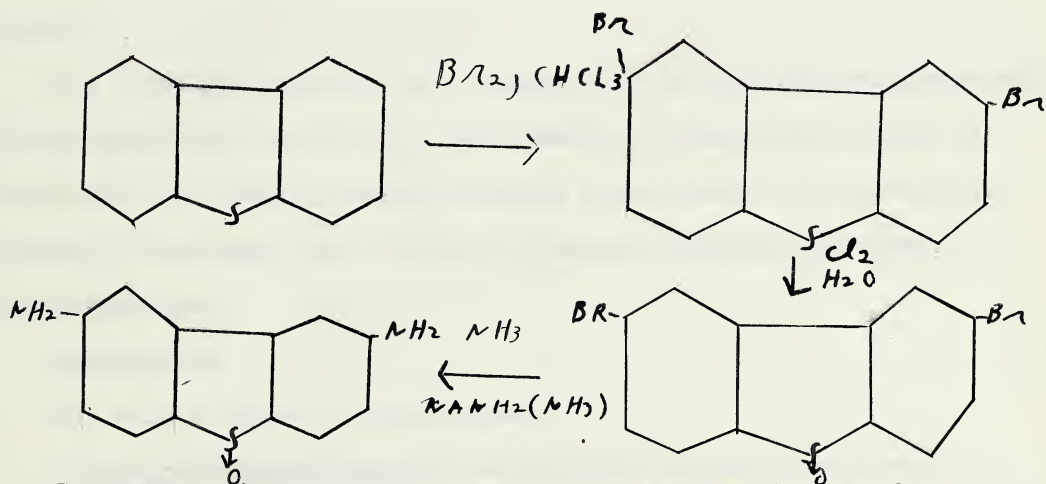
The system of numbering of dibenzothiophene is shown above. In most of its reactions dibenzothiophene is attacked at the 2- position. Using more strenuous conditions further reactions involves the 8- position. Thus it is known that the product of mono-nitration is the 2-nitro derivative, and in dinitration the product is the 2,8- compound (3). Similarly dibromination occurs in the 2,8- positions (4).

Two routes to synthesize the required compounds were tried. A flow sheet illustrating the two methods tried are shown below. Both methods were unsuccessful.





Route B



In route A 2,8-diacetaminodibenzothiophene was readily made although the overall yield starting from dibenzothiophene was small. Oxidation of it by means of hydrogen peroxide gave only compounds of indefinite melting points from which no sulfoxide could be isolated. Reaction of the diacetaminosulphide with chlorine and subsequent hydrolysis evidently gave ring chlorination.

In route B, 2,8-dibromodibenzthiophene-5-oxide was readily made by chlorinating and subsequent hydrolysis of the chlorine addition-product. Diamination of the dibromo-sulfoxide was tried with sodamide in liquid ammonia and also with ammonium hydroxide in a Carius bomb-tube. The first method gave a small yield of 2,8-diaminodibenzothiophene whereas the second method gave the same product, together with much tar, or, else unchanged dibromo-sulfoxide depending on the conditions used. Evidently the oxygen in the sulfoxide is very loosely held and is readily split off by reducing agents such as sodium amide and copper.

The 2,8-dibromo-sulphone gave a good yield of the 2,8-diamino-sulphone when treated with concentrated ammonia in a Carius bomb-tube. When treated with sodamide in liquid ammonia the dibromo-sulphone gave no indentifiable products.

The 2,8-dibromo-sulphide gave a small yield of 2,8-diamino-sulphide when it was treated with sodamide in liquid ammonia. Neumoyer and Amstutz (2) report that the 2,8-dibromo-sulphide gives a good yield of the 2,8-diamino-sulphide on treatment with concentrated ammonium hydroxide and copper in a Carius bomb-tube.

Experimental

All melting points are uncorrected.

2,8-Dibromodibenzothiophene. The procedure suggested by Courtot (4) was utilized. To a solution of 18.4 g. (0.1 mole) of dibenzothiophene dissolved in 200 cc. of chloroform, 11 cc. of bromine was added dropwise from a dropping funnel. The mixture was allowed to sit overnight after which the solvent was removed and 50 cc. of 95% ethyl alcohol was added and the product was filtered. Recrystallization from benzene yielded 13.0 g. (38%) of material melting at 220-221° (reported 229°) (4).

2,8-Dibromodibenzothiophene-5-oxide. An excess of chlorine was bubbled through 6.0 g. of 2,8-dibromodibenzothiophene, dissolved in 600 cc. of anhydrous benzene. The mixture was then poured into ice and water and shaken vigorously. The crude yield of sulfoxide that separated was 4.6 g. After several recrystallizations from benzene the melting point was 298-299°.

Anal. Calcd. for $C_{12}H_6OBr_2S$: S, 8.9. Found: S, 8.8.

Diamination of 2,8-Dibromodibenzothiophene-5-oxide A. A mixture of 2,8-dibromodibenzothiophene-5-oxide, 7.5 cc. of concentrated aqueous ammonia and a pinch of copper bronze was heated approximately ten hours at 200-230° in a carius bomb-tube. The material from the tube was filtered and the solid dissolved in dilute hydrochloric acid. This solution when made alkaline gave a precipitate which was filtered and washed with water. The solid melted at 191-192°. On admixture with an authentic sample prepared by Courtot's method (3), the substance showed no depression of the melting point. Similar aminations were tried using the same conditions except the catalyst was different. When cuprous chloride or cupric chloride were used, small yields of 2,8-diaminodibenzothiophene were obtained. When no catalyst was used only unchanged 2,8-dibromodibenzothiophene^{-5-oxide} was recovered.

B. Sodamide was prepared by the directions of Vaughn, Vogt and Niewland (5) from 2 g. of sodium and 0.1 g. of hydrated ferric nitrate in 200 cc. of liquid ammonia. Five grams of 2,8-dibromodibenzothiophene^{-5-oxide} was added and the mixture allowed to stand overnight. After allowing the ammonia to evaporate the solid remaining was extracted with dilute hydrochloric acid. On rendering the hydrochloric acid solution alkaline, a small yield of material melting at 191-192° was obtained. This compound gave no depression of the melting point when admixed with an authentic sample of 2,8-diaminodibenzothiophene (3).

2,8-Dibromodibenzothiophene-5-dioxide. Eight grams of 2,8-dibromodibenzothiophene, 10 cc. of concentrated sulfuric acid, 10 cc. of water and 10 g. of sodium dichromate were refluxed for two hours. After cooling, filtering and washing with water a yield of 8.5 g. of material melting 345° (reported 341°) (2) was obtained.

Diamination of 2,8-Dibromodibenzothiophene-5-dioxide A. A mixture of 1 g. 2,8-dibromodibenzothiophene-5-dioxide, 0.2 g. of copper bronze and 20 cc. of concentrated aqueous ammonium hydroxide was heated for ten hours at $200-230^{\circ}$ in a Carius bomb-tube. The contents of the tube were filtered and the solid dissolved in dilute hydrochloric acid. This hydrochloric acid solution was treated with norite, filtered and the filtrate made alkaline. One gram of pinkish material was obtained melting at 310° . Neumoyer and Amstutz report the melting point $329-331^{\circ}$ (corrected) (2).

B. When 2,8-dibromodibenzothiophene-5-dioxide was treated with sodamide in liquid ammonia under the same conditions as used for 2,8-dibromodibenzothiophene-5-oxide, no known products could be isolated.

Diamination of 2,8-Dibromodibenzothiophene A. 2,8-dibromodibenzothiophene when treated with concentrated ammonium hydroxide under conditions analogous to those for the corresponding 5-oxide, gave 2,8-diaminodibenzothiophene melting at 192° . This diamine gave no depression of the melting point with an admixture of an authentic sample.

B. 2,8-Dibromodibenzothiophene when treated with sodamide using the same conditions as those for the 5-oxide, gave a small yield of 2,8-diaminodibenzothiophene along with unreacted 2,8-dibromodibenzothiophene.

References

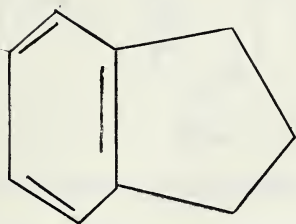
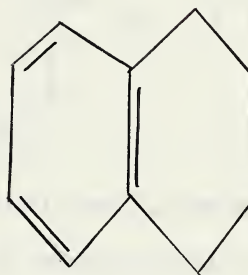
1. Boyland, Biochem. J., 32, 1207 (1938)
2. Neumoyer and Amstutz, J. Am. Chem. Soc., 69, 1920 (1947)
3. Courtot and Pomonis, Compt. rend., 182, 894 (1926)
4. Courtot, Nicolas and Liang., Compt. rend., 186, 1624 (1928)
5. Vaughn, Vogt and Nieuwland, J. Am. Che. Soc., 56, 2120 (1934)

Summary

The diamination of 2,8-dibromodibenzothiophene, 2,8-dibromodibenzothiophene-5-dioxide by concentrated ammonium hydroxide and by sodamide has been studied. The only previously unreported compound that has been made is 2,8-dibromodibenzothiophene-5-oxide.

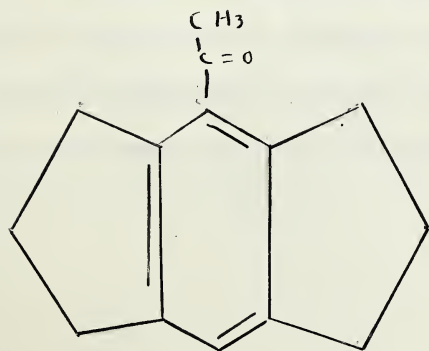
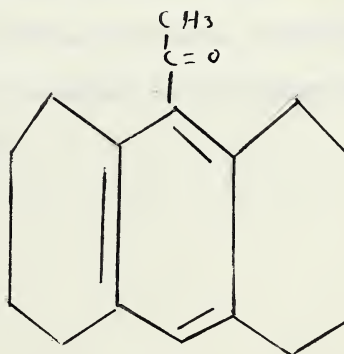
PART III

The Rates of Dissociation of 1,1,1,2-Tetraphenyl-2-(5-tetralyl)-ethane and 1,1,1,2-Tetraphenyl-2-(4-hydrindenyl)-ethane.

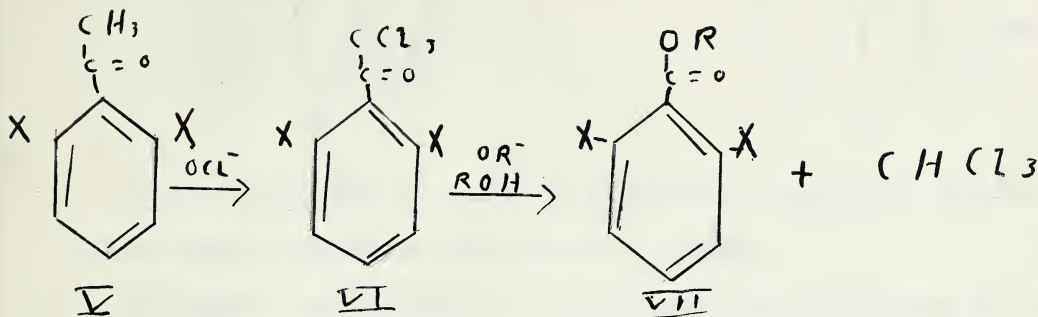
INTRODUCTION**I****II**

In their original paper, Mills and Nixon (1) pointed out that in hydrindene (I), the two bonds linking the trimethylene group to the benzenoid ring are probably distorted towards one another. A very important result that must accompany such a deflection of these valence bonds is a reduction in the steric influence of the methylene groups adjacent to the benzene ring. It follows that the steric effect of a five-membered ring should be smaller than that of a corresponding six-membered ring such as in tetralin (II).

Experimental support for this view was found by Arnold and Rondestvedt (2).

**III****IV**

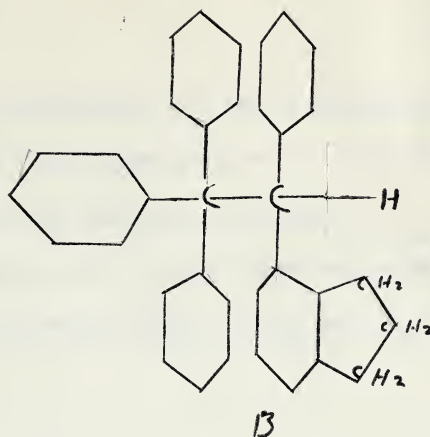
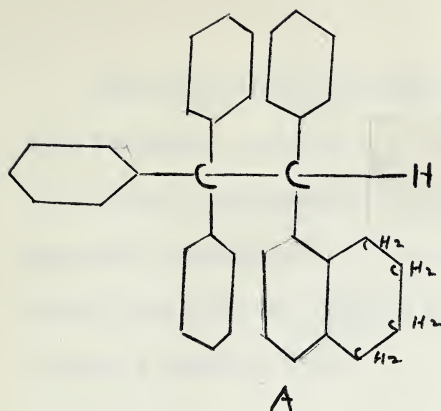
They found that 4-acetylhydrindacene (III) undergoes a normal haloform reaction whereas 9-acetyloctahydroanthracene (IV), acts like a highly hindered ketone and forms a relatively stable trichloro ketone. The mechanism of the haloform reaction can be described by the following equations (2).



If the ortho substituent "X" is sufficiently small, the haloform reaction proceeds rapidly to give chloroform and either an acid or its ester. When the group "X" is large enough (even methyl) the last step in the haloform reaction is sterically inhibited and the trichloro-ketone (VI) is isolated as the reaction product.

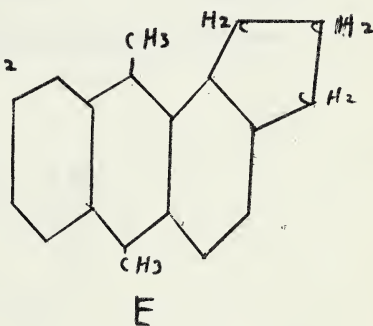
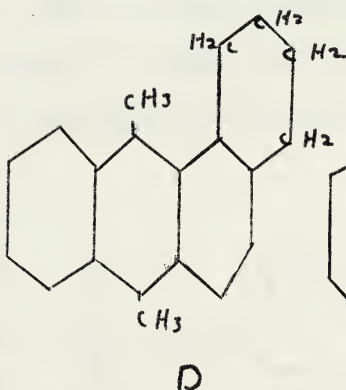
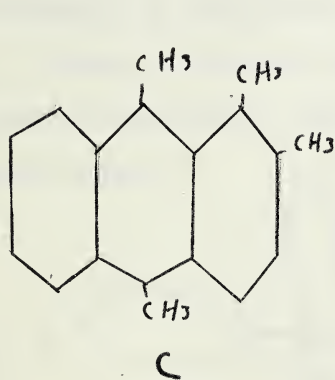
Arnold and Rondestvedt found that 4-acetylhydrindacene gave an acid and its methyl ester whereas 9-acetyloctahydroanthracene gave a stable trichloro ketone. In a later publication, Arnold and Rondestvedt (3), brought further evidence to support the view that the steric influence of an ortho methylene group in a six-membered ring is greater than in a five-membered ring.

Another possible way of testing for this steric difference should be by the comparison of the half-life periods of pentaaryl ethanes containing either a hydrindenyl group or a tetralyl group, attached to the ethane carbon in a position ortho to the methylene groups.



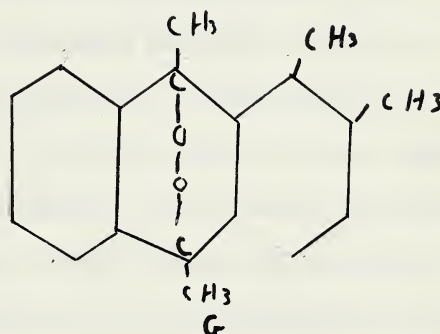
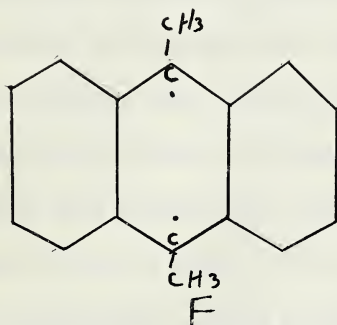
It was thought that it should be profitable to synthesize these two hydrocarbons and to determine their half-life periods.

The greater steric effect of a six-membered ring should mean that the tetralin hydrocarbon should dissociate much faster than the corresponding hydrindene hydrocarbon. This would mean the tetralin hydrocarbon should have a shorter half-life period.



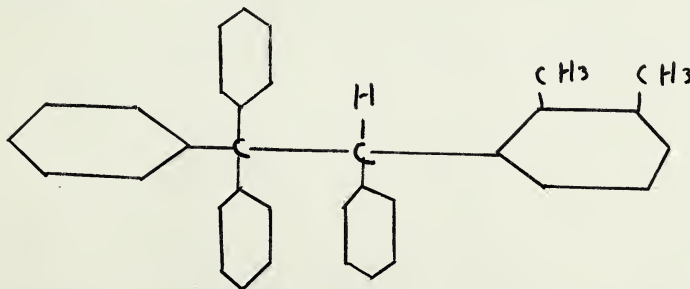
Another benefit of knowing the half-life periods of these hydrocarbons, would be that this knowledge should be applicable in determining qualitatively the relative stability of the three anthracene derivatives shown above.

The hydrocarbon 1,2,9,10-tetramethylantracene (C) was synthesized in 1943 by Sandin, Kitchen and Fieser (4). This hydrocarbon was highly sensitive to air and became oxygenated after brief periods of storage. The most plausible explanation of this sensitivity to air is that this hydrocarbon exists partly as an unstable biradical (F) which tends to pick up oxygen forming a peroxide (G).



The steric effect of a 1,2-dimethyl group might tend to reduce the coplanarity of the benzene rings and tends to stabilize structure F.

Grunert, Nichol and Sandin (5) studied the effect of a 1,2-dimethyl group by measuring the half-life period of 1,1,1,2-tetraphenyl-2-(3-o-xylyl)-ethane.



This hydrocarbon upon dissociation gives a structure similar to the biradical structure (F). As was expected the half-life period was found to be very short (13.4 minutes) indicating the 1,2-dimethyl group has a large

steric effect. By analogy the 1,2,9,10-tetramethylantracene should likewise contribute to the great reactivity of this compound.

By a comparison of the half-life periods of 1,1,1,2-tetraphenyl-2-(3-o-xylyl)-ethane, 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane and 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane, one should gain information concerning the relative stability of hydrocarbons C. D and E. If the half-life period of either the tetralyl or hydrindenyl hydrocarbon is less than that of the 3-o-xylyl hydrocarbon, the corresponding anthracene derivative should be more unstable than 1,2,9,10-tetramethylantracene and consequently its synthesis would likely be impossible. If the half-life period of either hydrocarbon were greater than the 3-o-xylyl hydrocarbon, the corresponding anthracene derivative should be more stable than 1,2,9,10-tetramethyl-anthracene and consequently should be easier to make than 1,2,9,10-tetramethylantracene.

The object of Part III of this thesis was to prepare 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane and 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane and to measure their half-life periods.

Theory of Pentaaryl Ethanes

The pentaarylethanes are colorless solids giving colorless solutions at room temperature. When the solution is heated to 80-100° a yellow color appears indicating that dissociation into free radicals has taken place. At 100° pentaaryl ethanes absorb oxygen, bromine and iodine very rapidly. The pentaphenylethanes are much more stable than the hexaphenylethanes which dissociate at room temperature.

From a study of the rate of oxygen absorption at 80-100°, it was established that pentaphenylethane undergoes dissociation in solution into diphenylmethyl and triphenylmethyl radicals (6)

Even in a colorless solution of pentaphenylethane this equilibrium exists. There is a rapid dissociation into free radicals which recombine, as quickly as they are formed, into pentaphenylethane.

The treatment of pentaarylethanes at 80-100° with oxygen results in the formation of unsymmetrical peroxides. This oxidation process was shown by Bachman and Wiselogle (6) to be a measure of the degree of dissociation of the pentaarylethane, i.e., the oxidation involves a slow dissociation of the pentaarylethane into free radicals, followed by a rapid conversion to the peroxide. The dissociation accordingly is the rate-controlling process.

$$\frac{dx}{dt} = k(a-x)$$

where $\frac{dx}{dt}$ = reaction rate

x is amount hydrocarbon reacted at time t.

a is the initial concentration of the hydrocarbon

(a-x) is the concentration of hydrocarbon at time t.

Integrating we get

$$-\ln(a-x) = kt + c$$

when t = 0, x = 0, ∴ c = -ln(a)

$$\therefore -\ln(a-x) = kt - \ln(a)$$

$$\therefore \ln(a) - \ln(a-x) = kt$$

$$\therefore \ln(a-x)/\ln(a) = -kt$$

$$\therefore \ln(1-x/a) = -kt$$

$$\therefore \ln(1-z) = -kt$$

where $z = x/a$

$$\therefore k = -1/t \ln(1-z)$$

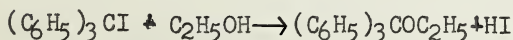
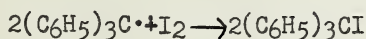
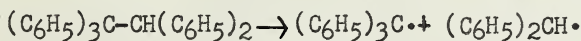
$$= -2.3/t \log(1-z)$$

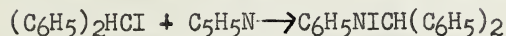
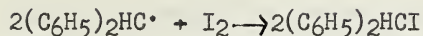
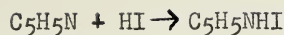
when hydrocarbon is half-dissociated

$$1-z = 0.5, \text{ and } t = t_{\frac{1}{2}}$$

$$\therefore t_{\frac{1}{2}} = \frac{-1}{k} \times 2.3 \log(0.5)$$

Bachman and Osborne (7) developed a good method for determining the rates of dissociation of pentaarylethanes. Instead of using oxygen, they allowed the pentaarylethane to react with iodine. The iodine was used in a solution of pyridine, o-dichlorobenzene and ethanol. The o-dichlorobenzene acted as an inert solvent. The ethanol converted the triphenylmethyl iodide to ~~tri-phenylmethyl iodide~~ triphenylmethyl ether as fast as it was formed. This was essential as the reaction of triphenylmethyl and iodine to give triphenylmethyl iodide is reversible. The pyridine was present to tie up with the hydrogeniodide (produced in the triphenylmethyl ether formation) in order to prevent it reacting with the free radicals. The diphenylmethyl iodide tied up with pyridine to give a quaternary salt in preference to forming an ether by a reaction with ethanol. The following equations illustrate the method.





Using this procedure Bachman and Osborn (7) found that the dissociation into free radicals was again the rate-controlling process, being first order and unimolecular. Hence we can apply the formula derived previously.

$$k = -2.3/t \log(1-z)$$

Where z = fraction of pentaaryl dissociated = ratio of the amount of iodine adsorbed at time t to the theoretical absorption.

By plotting t against $-\log(1-z)$ and drawing the best-fitting straight line and calculating the slope, we can find k and also the half-life period.

$$\text{slope} = k/2.3$$

$$\therefore k = 2.3 \times \text{slope}$$

$$t_{1/2} = \log 2 / \text{slope}$$

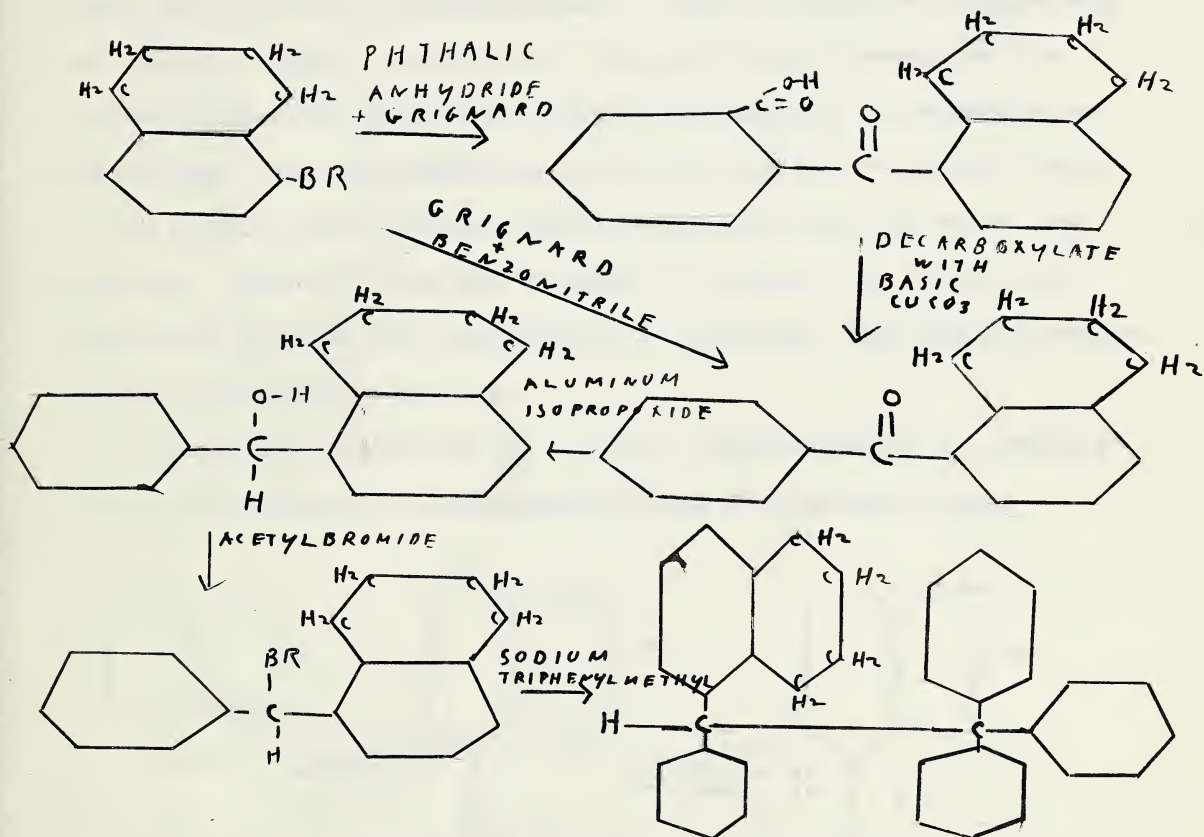
$$= 0.3010 / \text{slope}$$

Using this method Bachman and coworkers (7,8) determined the half-life period of a great number of pentaarylethanes. These workers found the effect of replacing one or more phenyl groups in pentaphenylethane by other groups. Grunert, Nichol and Sandin (4) studied the effect of xyllyl groups on the degree of dissociation.

DISCUSSION

Half-life periods of pentaphenylethane were run until a value close to that determined by Bachman (7) was obtained. This was thought necessary in order to be sure the technique used was accurate enough.

A flow sheet below illustrates the procedure used to synthesize 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane.

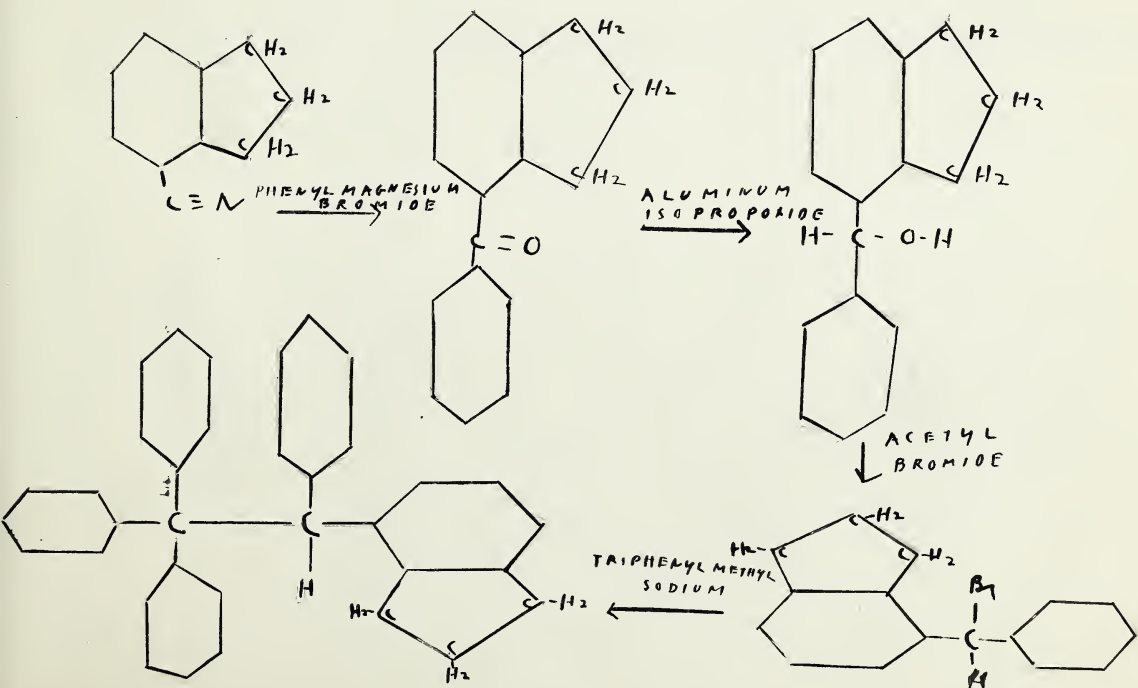


2-(5-Tetraloyl)-benzoic acid was made in good yield by a Grignard reaction with phthalic anhydride. The keto-carboxylic acid was readily decarboxylated by basic copper carbonate giving a good yield of 5-benzoyltetralin. The latter compound was also made by the action of the Grignard from 5-bromotetralin on benzonitrile.

This ketone was converted to phenyl-5-tetralylcarbinol by the action of aluminum isopropoxide (10,11). This carbinol could not be obtained by the action of the Grignard reagent made from 5-bromotetralin on benzaldehyde. The oil produced by this reaction gave low carbon-hydrogen analytical results.

Phenyl-5-tetralylmethyl bromide was made by the action of acetyl bromide on the carbinol. It was coupled immediately with sodium triphenylmethyl to give a good yield of the pentaarylethane. When the carbinol was treated with 30% hydrogen bromide in acetic acid, followed by acetyl bromide and then vacuum distilled and coupled with sodium triphenylmethyl, no pentaarylethane was obtained. The only explanation possible was the loss of hydrogen bromide at some stage. This would most likely have occurred during the vacuum distillation. Bachman, Hoffman and Whitehead (8) reported that some of their diarylmethyl bromides were too unstable to be distilled. They used the bromides without purification or analysis.

A flow sheet illustrating the series of reactions used in the synthesis of 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane is illustrated below.



4-cyanohydrindine was prepared according to the direction of Fieser and Hershberg (12). A good yield of 4-benzoylhydrindene was obtained by the reaction of phenyl magnesium bromide on 4-cyanohydrindene. The ketone was readily reduced to phenyl-4-hydrindenyl carbinol by means of aluminum isopropoxide (10,11). The carbinol when treated with acetyl bromide and then coupled with sodium triphenylmethyl, gave a good yield of 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane.

EXPERIMENTAL

All melting points and boiling points are uncorrected.

5-Bromotetralin. This compound was made according to the directions of Fieser and Hershberg (9).

2-(5-Tetraloyl)-benzoic acid. This compound was made by the action of the Grignard reagent prepared from 5-bromotetralin on phthalic anhydride, according to the directions of Fieser and Hershberg (9).

5-Benzoyltetralin A. From 2-(5-tetraloyl)-benzoic acid. Sixty grams of 2-(5-tetraloyl)-benzoic acid was heated with a free flame in a 125 cc. Claissen distilling glask to 200° to eliminate all moisture. A thermometer was inserted in the hot acid. The acid was cooled and 1 g. of basic copper carbonate was added. The mixture was heated rapidly to 265° by means of a salt bath and kept at this temperature until no more carbon dioxide was evolved. The 5-benzoyltetralin was then vacuum distilled giving 30 g. (60%) of a viscous oil which did not solidify on long standing. b.p. 215-217° (10 mm.)

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 86.52; H, 6.60.

B. From reaction of Grignard reagent from 5-bromotetralin on benzonitrile. The Grignard reagent prepared from 30.0 g. of 5-bromotetralin, dissolved in ether and benzene was added to freshly distilled benzonitrile. The mixture was refluxed for several hours. The precipitate that formed did not go into solution. The benzene and ether were evaporated and hydrochloric acid added to the residue. The mixture was refluxed for five hours, then extracted with ether. After removing the ether, the residue was vacuum distilled giving 14 g. (41%) of a viscous oil identical with that obtained by decarboxylating 2-(5-tetraloyl)-benzoic acid.

Phenyl-5-tetralylcarbinol. Eight grams of aluminum wire cleaned by emery paper, was placed in a 500 cc. florence flask to which was attached a Tamworth condenser fitted with a calcium chloride drying tube. The flask was heated with a free flame to drive off any moisture. A pinch of mercuric chloride, 1 cc. of carbontetrachloride and 200 cc. of dry isopropyl alcohol was then added and the mixture refluxed for eight hours. The mixture was filtered through a cotton plug into a 500 cc. clean dry florence flask. The isopropyl alcohol was distilled off and 30 g. of 5-benzoyltetralin dissolved in 250 cc. of dry toluene was added and the mixture was refluxed for seven hours. A Snyder column was now attached in place of the condenser and 100 cc. of dry isopropyl alcohol was added and fractionally distilled over a period of several hours. Another 100 cc. of dry isopropyl alcohol was added and fractionally distilled. The solution was hydrolysed by cold 10% sulfuric acid and the toluene layer dried over anhydrous sodium sulphate. The toluene was distilled off and the residue vacuum distilled giving 20 g. (66%) of a yellow viscous oil. b.p. 225-229° (12 mm.), 174-175° (1.5 mm.)

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.23; 85.20; H, 7.45; 7.50.

Phenyl-5-tetralylmethyl Bromide. A mixture of 8 g. of the above carbinol, 15 cc. of acetyl bromide and 20 cc. of benzene was refluxed on a water bath for one hour. The solvents were removed under reduced pressure and then benzene was added and distilled off. This was repeated twice so that all acetyl bromide was removed. This bromo-compound was used directly without further purification.

1,1,1,2-Tetraphenyl-2-(5-tetralyl)-ethane. To 45 g. of molten sodium under xylene in a 250 cc. Erlenmeyer flask 55 g. of mercury was added slowly through

a pin-point hole in a filter-paper. The amalgam was pipetted out and placed under dry benzene in a glass-stoppered bottle.

To this amalgam, contained in a 500 cc. glass-stoppered bottle was added 10.0 g. of triphenylchloromethane dissolved in 50 cc. of benzene and 50 cc. of ether. The bottle was sealed with a special stop-cock grease (13), cooled in an ice-bath and shaken by hand. After several hours of intermittent shaking the amalgam was frozen by immersing in an ice bath. The unpurified phenyl-5-tetralylmethyl bromide was quickly added and the glass-stoppered bottle was shaken. The solution was transferred to a separatory funnel by decantation and ethanol cautiously added to destroy any unreacted amalgam. The benzene layer was washed with water and dried for a short time over anhydrous sodium sulphate. Methanol was added to the benzene causing the hydrocarbon to precipitate. A yield of 11 g. was obtained. On recrystallizing from benzene and methanol 6.5 g. of material melting at 190-194° was obtained. The crystals were dried in vacuo for three hours before a carbon-hydrogen analysis was run.

Anal. Calcd. for $C_{26}H_{32}$: C, 93.07; H, 6.94. Found: C, 92.85; H, 7.02.

4-Cyanohydrindene. This compound was prepared according to the directions of Fieser and Hershberg (12).

4-Benzoylhydrindene. A yield of 17 g. (63.5%) of 4-benzoylhydrindene was obtained from the action of phenylmagnesiumbromide on 17 g. of 4-cyanohydrindene. This oil was viscous but would not solidify on long standing. b.p. 177-180° (2 mm.).

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.44; H, 6.35. Found: C, 86.76; H, 6.47

Phenyl-4-hydrindenylcarbinol. A yield of 9 g. (53%) of phenyl-4-hydrindenylcarbinol was obtained from 17 g. of 4-benzoylhydrindene using aluminum isopropoxide as the reducing agent in an analogous manner to the reduction of 5-benzoyltetralin. b.p. 180° (4 mm.).

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.69; H, 7.19. Found: C, 85.84; H, 7.17.

Phenyl-4-hydrindenylmethyl Bromide. This compound was made from the above carbinol by means of acetyl bromide in a similar manner to the preparation of phenyl-5-tetralylmethyl bromide.

1,1,1,2-Tetraphenyl-2-(4-hydrindenyl)-ethane. The procedure followed was the same as for 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane. A yield of 11.0 g. hydrocarbon was obtained from 9.0 g. of carbinol. After the hydrocarbon was recrystallized from benzene and methanol it melted at 185-190°.

Anal. Calcd. for $C_{35}H_{30}$: C, 93.29; H, 6.71. Found: C, 93.44; H, 6.90.

Half-life Period of Pentaphenylethane. For standardizing technique check runs were made on the half-life of pentaphenylethane prepared by the procedure of Bachman (14). Results obtained were 53.1 minutes, 37.3 minutes and 55.3 minutes. The second half-life is distinctly in error. The reason for this discrepancy is most likely due to poor distilled water. It was found that the distilled water system was being contaminated by improper joints. The last value (55.3) is in good agreement with the value (56.0 min.) determined by Bachman (7).

Half-life Period of 1,1,1,2-Tetraphenyl-2-(5-tetralyl)-ethane.

Rate Measurements. The iodine solution was made up by adding o-dichlorobenzene to a solution of 6.5 g. of iodine in 32.5 cc. of pyridine until the total volume was 500 cc. The sodium thiosulphate was made slightly stronger than 0.1N so that it would be strong enough to react with all the iodine originally present in the organic iodine solution. The aqueous iodine solution was 0.1N in strength and was standardized against arsenious oxide.

The samples (0.1162 g. each) were weighed into glass vials about 12 mm. deep and 8 mm. in diameter, with flat bottoms. Ten cubic centimeters of

organic iodine solution and 1 cc. of absolute methanol were placed in a 125 cc. glass-stoppered Erlenmeyer flask. The flask was suspended in a water bath (with a coating of oil to prevent excessive evaporation) kept at 80° to within 0.1° . The vial containing the sample of pentaphenylethane was then lowered in an upright position into the Erlenmeyer flask by means of forceps and allowed to float on the surface of the organic solution of iodine. The flask after being stoppered loosely was allowed to reach the temperature of the bath by allowing it to sit for ten minutes. The vial was then tipped over by swirling the flask, a stop-watch being started at this time. When the desired interval of time had elapsed, the flask was removed from the bath and immersed in ice-water, the watch being stopped at this point.

The flask was kept in ice water for one minute and then 10 cc. of sodium thiosulphate solution was added. The solution was well mixed for half a minute, the sides of the flask washed down with 50 cc. of water and the excess sodium thiosulphate titrated with the standardized 0.1N solution of iodine. From the volume of this standard iodine solution needed to give the end-point with starch (3 cc. of a 1% solution) was subtracted the volume of iodine solution required to give the end-point to a blank. The latter was run with all the reagents except the pentaphenylethane in exactly the same manner as a regular run. The difference was the volume of 0.1N iodine which reacted with the free radicals formed by dissociation of the 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane.

Knowing the concentration of the standardized iodine solution, the volume theoretically absorbed by 0.1162 g. of the tetralyl-ethane was calculated. Calculations were then carried out and values for t were plotted against $-\log(1-\frac{t}{\tau})$. The best fitting straight line was drawn, its slope determined, and the half-life period was calculated.

It was found that the presence of an appreciable amount of phenyl-5-tetralyl-methyl-pyridinium iodide in the aqueous solution interfered with the end point. For this reason only short time intervals were taken. For some reason the best-fitting straight line did not go through the origin, the reason for this is not known.

The tabulated results together with their respective graphs of two runs are given.

Wt., of 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane, 0.1162 g.

o-dichlorobenzene, 89.3 %, pyridine, 4.7 %, methanol, 6 %.

Theoretical absorption of 0.0996 N iodine, 5.02 cc.

Temperature, 80.0 + 0.1°.

Run number 1

Time	cc. of Iodine abs.	z (found)	$-\text{Log}(1-z)$
1	0.16	0.0318	0.0140
2	0.41	0.0817	0.0371
3	0.59	0.1175	0.0543
3	0.82	0.1632	0.0774
4	1.00	0.1990	0.0964
4	1.02	0.2030	0.0985
5	1.36	0.2708	0.1372

Run number 6

Conditions the same except that the strength of the iodine solution was 0.1049, and consequently the theoretical absorption of iodine was 4.77 cc..

Time	cc. of Iodine abs.	z (found)	$-\text{Log}(1-z)$
1.5	0.29	0.0608	0.0272
2.0	0.48	0.1005	0.0460
2.5	0.61	0.1277	0.0594
3.0	0.76	0.1591	0.0752
3.5	0.86	0.1800	0.0852
4.0	1.02	0.2140	0.1046

Time was plotted against $-\log(1-z)$ and the best-fitting straight line was drawn. The slope was calculated and from the slope the half-life period and K were obtained.

1. The first part of the report is a general introduction to the subject of the study. It discusses the importance of the study and the objectives of the research.

2. The second part of the report is a detailed description of the methodology used in the study. It includes information about the sample size, the data collection methods, and the statistical analysis techniques.

3. The third part of the report is a presentation of the results of the study. It includes tables and graphs showing the data and the statistical analysis.

4. The fourth part of the report is a discussion of the results and their implications. It discusses the strengths and limitations of the study and the implications for future research.

Appendix A

Name	Address	Phone Number	Date
John Doe	123 Main St	555-1234	1/1/2020
Jane Smith	456 Elm St	555-5678	1/2/2020
Bob Johnson	789 Oak St	555-9012	1/3/2020
Alice Brown	101 Pine St	555-3456	1/4/2020
Charlie White	202 Cedar St	555-7890	1/5/2020
David Black	303 Birch St	555-2345	1/6/2020
Emily Green	404 Spruce St	555-6789	1/7/2020

Appendix B

This appendix contains a list of references used in the study. The references are listed in alphabetical order by the author's name.

1. Smith, J. (2018). The impact of social media on mental health. *Journal of Social Media Research*, 1(1), 1-10.

2. Doe, A. (2019). The effects of stress on physical health. *Stress and Health*, 35(2), 123-135.

3. Johnson, B. (2020). The role of exercise in mental health. *Exercise and Mental Health*, 15(1), 45-55.

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Emily Green	404 Spruce St	555-6789	1/7/2020

Values of the half-life period that were obtained were:

9.5, 10.0, 10.6, 12.0, 10.6 and 9.6 minutes.

The corresponding values of K were: 0.073, 0.069, 0.065, 0.065, 0.058 and 0.072 / minutes.

Half-life Period of 1,1,1,2-Tetraphenyl-2-(4-hydrindenyl)-ethane.

Rate Measurements. Rate measurements were made exactly as they were made for the tetralyl-hydrocarbon except that the size of sample was 0.1127 g., so that an equimolar amount of sample was used in each case. The time was also run up to eight minutes without running into difficulties with the end-point. The tabulated result of run number 2 is given together with the accompanying graph.

Run number 2

Same conditions as run number 6 for the tetralyl-hydrocarbon.

Time	cc. of Iodine abs.	γ (found)	$-\log(1-\gamma)$
1	0.18	0.0378	0.0167
2	0.34	0.0713	0.0322
3	0.41	0.0859	0.0391
4	0.55	0.1150	0.0531
5	0.65	0.1360	0.0635
6	0.72	0.1455	0.0682
7	0.84	0.1760	0.0841
8	0.95	0.1990	0.0964

Values of the half-life period obtained from the two runs were:

28.7 and 27.9 minutes. The corresponding values for K were:
0.0242 and 0.0250/minutes.

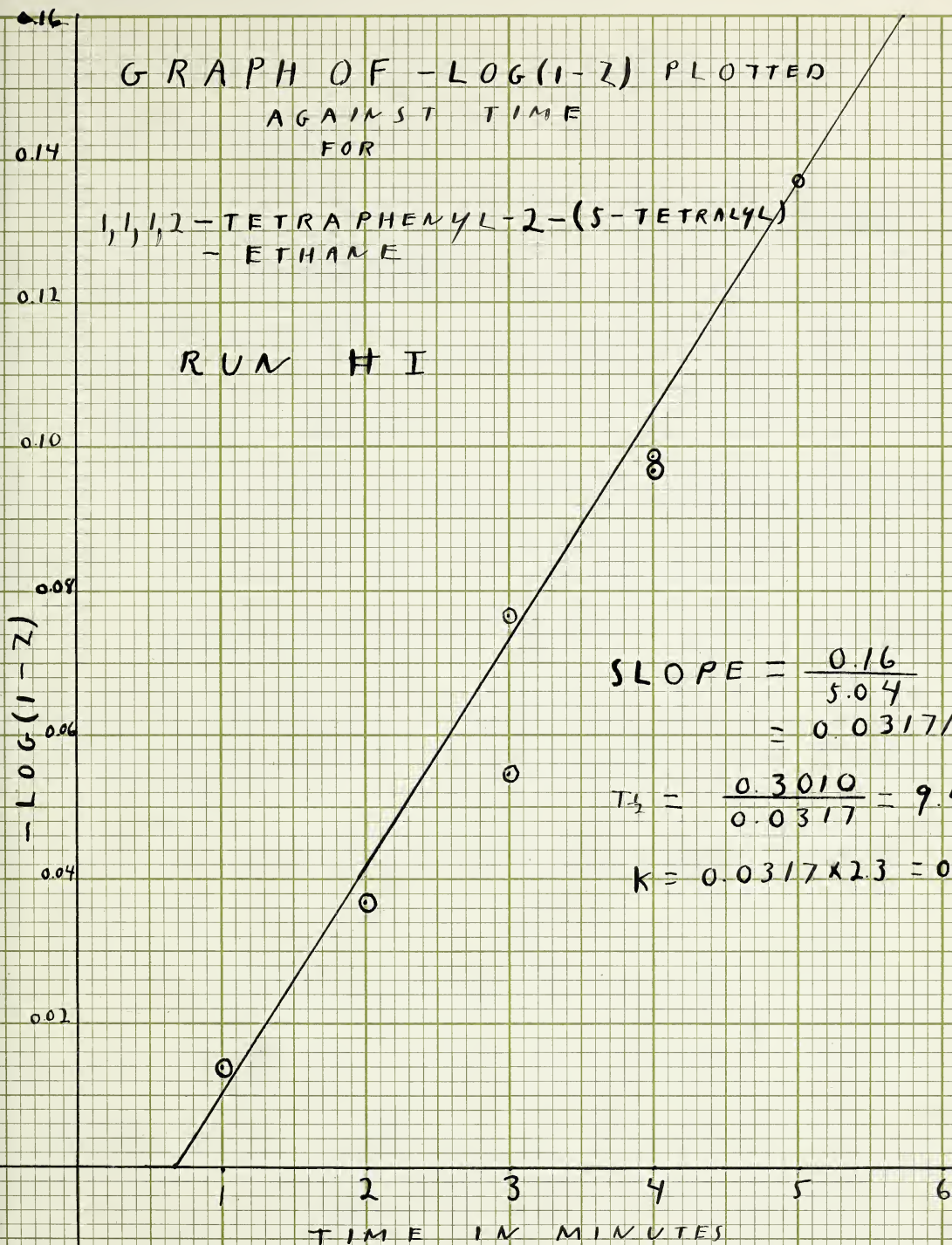
The average value obtained for the half-life of the
tetralyl-hydrocarbon was 10.4 minutes and the corresponding
value of K was 0.067/minutes.

The average value of the half-life for the hydrindenyl-
-hydrocarbon was 28.3 minutes and the corresponding value
for K was 0.0246/minutes.

GRAPH OF $-\log(1-Z)$ PLOTTED
AGAINST TIME
FOR

1,1,1,2-TETRAPHENYL-2-(5-TETRALYL)
- ETHANE

RUN HI



$$\text{SLOPE} = \frac{0.16}{5.04} = 0.0317/\text{MIN.}$$

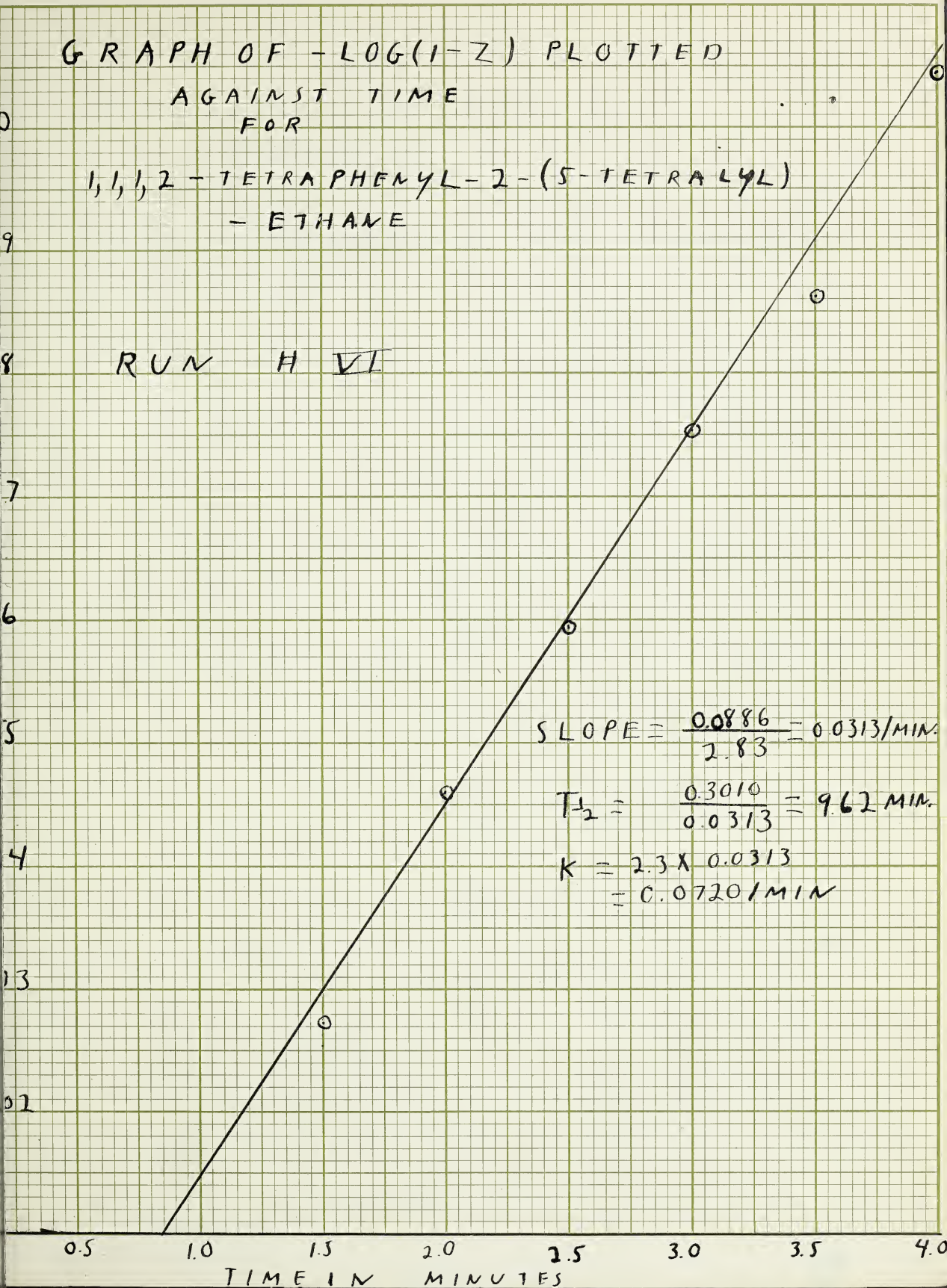
$$T_{1/2} = \frac{0.3010}{0.0317} = 9.48 \text{ MIN.}$$

$$K = 0.0317 \times 2.3 = 0.073/\text{MIN.}$$

GRAPH OF $-\log(1-Z)$ PLOTTED
AGAINST TIME
FOR

1,1,1,2-TETRA PHENYL-2-(5-TETRALYL)
- ETHANE

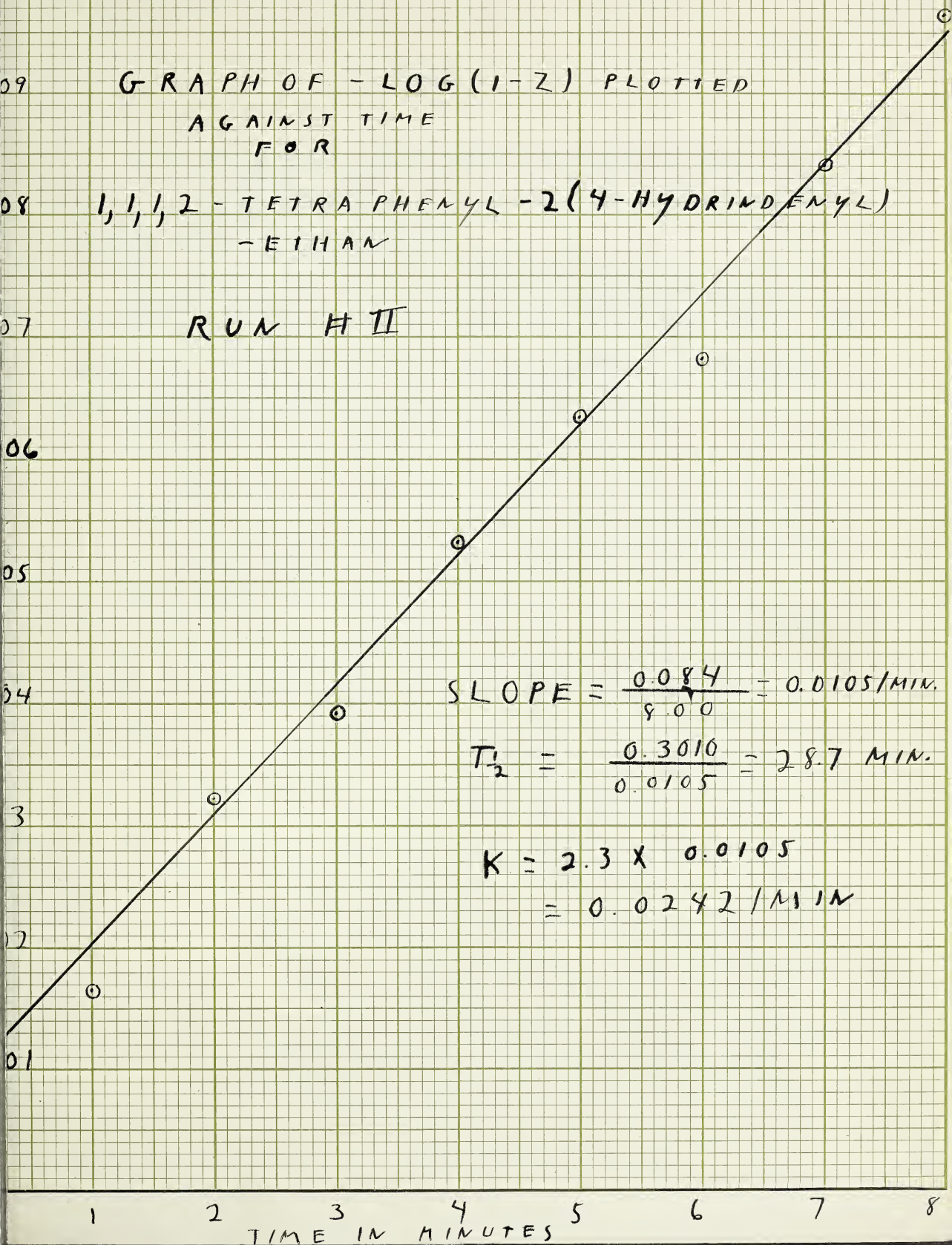
RUN H VI



GRAPH OF $-\log(1-Z)$ PLOTTED
AGAINST TIME
FOR

1,1,1,2-TETRA PHENYL-2(4-HYDRINDENYL)
-ETHAN

RUN H II



SUMMARY

The two hydrocarbons 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane and 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane have been synthesized and their half-life period has been determined.

The half-life period of 1,1,1,2-tetraphenyl-2-(5-tetralyl)-ethane is much shorter than that of 1,1,1,2-tetraphenyl-2-(4-hydrindenyl)-ethane. This agrees well with the supposition that the steric effect of a five-membered ring should be much less than that of a six-membered ring.

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